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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,734	12/15/2005	Timo Heinrich	MERCK-3099	3735
23599	7590	07/23/2008	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			JARRELL, NOBLE E	
			ART UNIT	PAPER NUMBER
			1624	
			MAIL DATE	DELIVERY MODE
			07/23/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/560,734	HEINRICH ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Noble Jarrell	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 24 April 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-4,6-9 and 11-14 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-4,6-9,11-14 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Response to Arguments***

1. The rejection 35 U.S.C. 101 and 112 has been overcome by the amendment filed 4/24/2008.
2. The rejections under 35 U.S.C. 102 have been overcome by the amendment filed 4/24/2008.
3. The rejection under 35 U.S.C. 103 has been overcome by the amendment filed 4/24/2008.
4. The double patenting rejections (obvious type) have been overcome by the amendment filed 4/24/2008.

### ***Claim Rejections - 35 USC § 112***

5. Claims 1-4, 6-9, and 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts or stereoisomers of compounds embraced by formula I, does not reasonably provide enablement for solvates of same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Vippagunta et al. (*Advanced Drug Delivery Reviews*, 2001, 48, 3-26, cited in previous office action) teach that solvate or hydrate formation is unpredictable among a series of related compounds because each compound responds uniquely to solvate or hydrate formation (page 18, section 3.4). This rejection is maintained because applicants have not given adequate guidance that compounds they have prepared can form solvates.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8

USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds with a piperazine or piperidine ring connected to one, an indoline ring through an alkyl linker, and two, a benzofuran ring through zero to four carbons, and compositions containing the same.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Vippagunta et al. teach that solvate or hydrate formation is unpredictable among a series of related compounds because each compound responds uniquely to solvate or hydrate formation (page 18, section 3.4).

*(5) The relative skill of those in the art:*

One of ordinary skill in the art can make a salt or stereoisomer of a compound of formula I. Mixtures of these two forms can be prepared as racemates as final products of a reaction.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for preparation of a salt or stereoisomer of a compound of formula I.

However, the specification does not provide guidance that any solvate can be prepared.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-4,6-9, and 11-14 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

6. Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of depression (major depressive disorders), does not reasonably provide enablement for treatment of any other disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants are enabled for treatment of major depressive disorders (Farvolden et al., *Expert Opinion on Investigational Drugs*, 2003, 12(1), 65-86, sections 5.1 (page 68) and 9.1 (pages 72-74)).

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to a method of inhibiting 5-HT<sub>1A</sub> receptors and/or serotonin reuptake with compounds of formula I.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Farvolden et al. teach inhibition of 5-HT<sub>1A</sub> receptors is associated with treatment of depression.

*(5) The relative skill of those in the art:*

One of ordinary skill in the art can replicate the assay done in example 5 (page 23) of the specification.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for the treatment of depression.

However, the specification does not provide guidance for any other disorders listed in claims 12-13.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to claims 12-13 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim(s) 11 is unclear as to its intended scope. Such claim language reciting inhibitory activity is generally used to denote a causative factor in determining the process by which a particular disease occurs. Determining whether a given disease responds or not to inhibition of a serotonin receptor and/or serotonin reuptake involves much experimentation since a negative response from one patient does not mean the drug isn't useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? Applicants cite (page 14, line 13- page 15, line 11) many diseases that could be associated with inhibition of either a serotonin receptor and/or serotonin reuptake. The test for determining compliance with 35 USC 112, paragraph two, is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

10. Regarding claim 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

### ***Conclusion***

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/  
Examiner, Art Unit 1624

/James O. Wilson/  
Supervisory Patent Examiner, Art Unit 1624